

IN THE CLAIMS

Please cancel claims 8, 30 and 40-48, without prejudice.

Please amend the claims as follows:

1. (Amended) A pharmaceutical composition, comprising a mixture of alpha interferon polymer conjugate positional isomers, wherein one of said positional isomers comprises an alpha interferon covalently conjugated to a substantially non-antigenic polymer at a histidine residue on said alpha interferon, wherein said substantially non-antigenic polymer is a polyalkylene oxide comprising an alkyl terminal.

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7. (Amended) The pharmaceutical composition of claim 6, wherein said alpha interferon is alpha interferon 2b and [the] said mixture of positional isomers [are selected from the group consisting of] comprises a substantially non-antigenic polymer linked to said alpha interferon 2b, at an amino acid residue selected from the group consisting of Cys1, Lys31, His34, Lys49, Lys83, Lys121, Lys131 and Lys134.

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8. (Amended) The pharmaceutical composition of claim [8] 1, wherein said polyalkylene oxide is a polyethylene glycol.

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10. (Amended) The pharmaceutical composition of claim [8] 2, wherein said polyalkylene oxide is a monomethoxy-polyethylene glycol, (mPEG).

11  
14. (Amended) A pharmaceutical composition, comprising a mixture of alpha interferon polymer conjugate positional isomers [The pharmaceutical composition of claim 1], wherein one of said positional isomers comprises an alpha interferon covalently conjugated to a [said polymer is] substantially non-antigenic polymer at a histidine residue on said alpha interferon, wherein said substantially non-antigenic polymer is selected from the group consisting of polypropylene glycol, dextran, polyvinyl pyrrolidones, polyacryl amides, polyvinyl alcohols and carbohydrate-based polymers.

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15. (Amended) An alpha interferon-containing composition, comprising a plurality of alpha interferon polymer conjugates, wherein at least about 15% of the conjugates include covalent attachment of [said] a substantially non-antigenic polymer at a histidine of said alpha interferon, wherein said substantially non-antigenic polymer is a polyalkylene oxide comprising an alkyl terminal.

18. (Amended) A pharmaceutical composition, comprising a mixture of alpha interferon 2b-polymer positional isomers, wherein from about 30 to about 60% of the positional isomers include a substantially non-antigenic polymer conjugated to the His34 of said alpha interferon, from about 7 to about 20% of the positional isomers include a substantially non-antigenic polymer conjugated to the Cys1 of said alpha interferon and about 7 to about 15% of the positional isomers include a substantially non-antigenic polymer conjugated to the Lys121 of said alpha interferon, wherein said substantially non-antigenic polymer is a polyalkylene oxide comprising an alkyl terminal.

19. (Amended) A method of preparing alpha-interferon conjugates, comprising contacting an alpha interferon with a sufficient amount of [an] a mono-activated oxycarbonyl-oxy-N- dicarboximide-activated substantially non-antigenic polymer under conditions which are sufficient to facilitate covalent attachment of said substantially non-antigenic polymer at a histidine of said alpha interferon, wherein said substantially non-antigenic polymer is selected from the group consisting of a polyalkylene oxide comprising an alkyl terminal, polypropylene glycol, dextran, polyvinyl pyrrolidones, polyacryl amides, polyvinyl alcohols and carbohydrate-based polymers.

20. (Amended) The method of claim [26] 21, wherein said polymer is present in a molar excess] ratio ranging [is] from about 1 part polymer to about [8-fold] 8-parts alpha interferon.

21. (Amended) The method of claim [27] 26, wherein said polymer molar excess is from about 1.5 to about 7-fold.

22. (Amended) The method of claim [30] 21, wherein said polyalkylene oxide is a polyethylene glycol.

Please enter the following new claims:

23. (New) The pharmaceutical composition of claim 14, wherein said alpha interferon is interferon alpha 2b.

24. (New) The pharmaceutical composition of claim 49, wherein said histidine residue is His34.

25. (New) The pharmaceutical composition of claim 14, wherein said mixture of said alpha interferon positional isomers comprises at least about 3 positional isomers.

<sup>44</sup>  
<sup>52</sup>. (New) The pharmaceutical composition of claim <sup>13</sup>~~14~~, wherein said mixture of said alpha interferon positional isomers comprises at least about 6 positional isomers.

<sup>45</sup>  
<sup>53</sup>. (New) The pharmaceutical composition of claim <sup>13</sup>~~14~~, wherein said mixture of said alpha interferon positional isomers comprises at least about 8 positional isomers.

<sup>43</sup>  
<sup>54</sup>. (New) The pharmaceutical composition of claim <sup>38</sup>~~19~~; wherein said mixture of positional isomers comprises a substantially non-antigenic polymer linked to said alpha interferon 2b, at an amino acid residue selected from the group consisting of Cys1, Lys31, His34, Lys49, Lys83, Lys121, Lys131 and Lys134.

<sup>46</sup>  
<sup>55</sup>. (New) The pharmaceutical composition of claim <sup>13</sup>~~14~~, wherein said substantially non-antigenic polymer has a molecular weight of from about 200 to about 35,000.

<sup>45</sup>  
<sup>56</sup>. (New) The pharmaceutical composition of claim <sup>13</sup>~~14~~, wherein said substantially non-antigenic polymer has a molecular weight of from about 1,000 to about 15,000.

<sup>47</sup>  
<sup>57</sup>. (New) The pharmaceutical composition of claim <sup>13</sup>~~14~~, wherein said substantially non-antigenic polymer has a molecular weight of from about 2,000 to about 12,500.

<sup>48</sup>  
<sup>58</sup>. (New) The pharmaceutical composition of claim 1 wherein said polyalkylene oxide is terminated with a C<sub>1-4</sub> alkyl.

<sup>49</sup>  
<sup>59</sup>. (New) The pharmaceutical composition of claim <sup>18</sup>~~19~~ wherein said polyalkylene oxide is terminated with a C<sub>1-4</sub> alkyl.

<sup>50</sup>  
<sup>60</sup>. (New) The method of claim <sup>20</sup>~~21~~ wherein said polyalkylene oxide is terminated with a C<sub>1-4</sub> alkyl.

<sup>51</sup>  
<sup>61</sup>. (New) A pharmaceutical composition, comprising a mixture of alpha interferon polymer conjugate positional isomers, wherein at least one of said positional isomers comprises an alpha interferon covalently conjugated to a substantially non-antigenic polymer at a histidine residue on said alpha interferon, prepared by a process comprising contacting an alpha interferon with a sufficient amount of a mono-activated <sup>substantially</sup> non-antigenic polymer under conditions which are sufficient to facilitate covalent attachment of said substantially non-antigenic polymer at a histidine of said alpha interferon, said mono-activated substantially non-antigenic polymer being a polyalkylene oxide comprising <sup>an</sup> at least one alkyl substituted terminal.